

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Applicant: Paul A. RENHOWE et al.  
Title: HETEROCYCLIC COMPOUNDS  
Prior Appl. No.: 10/452,786  
Filing Date: Submitted Herewith  
Examiner: Unknown  
Art Unit: Unknown

**INFORMATION DISCLOSURE STATEMENT**  
**UNDER 37 CFR §1.56**

Mail Stop PATENT APPLICATION  
Commissioner for Patents  
PO Box 1450  
Alexandria, Virginia 22313-1450

Sir:

Applicants submit herewith on Form PTO-1449 a listing of the documents cited by or submitted to the U.S. PTO in parent application Serial No. 10/452,786, filed June 02, 2003, and parent application Serial No. 09/943,382, filed August 30, 2001. As provided in 37 CFR §1.98(d), copies of the documents are not being provided since they were previously submitted to the United States Patent & Trademark Office in the above-identified parent application.

The USPTO has waived the requirement under 37 CFR 1.98(a)(2)(i) to submit copies of U.S. patents and U.S. patent application publications when citing and submitting an Information Disclosure Statements in a patent application filed after June 30, 2003, and in an international application that has entered the national stage under 37 USC §371 after June 30, 2003. Accordingly, copies of these types of documents are not being supplied in connection with this application. Reference is being made to Pre-OG Notice from Office of Patent Legal Administration dated July 25, 2003, *Information Disclosure Statements May Be Filed Without Copies of U.S. Patents and Published Applications in Patent Applications filed after June 30, 2003.*

The submission of any document herewith, which is not a statutory bar, is not intended as an admission that such document constitutes prior art against the claims of the present application or that such document is considered material to patentability as defined in 37 CFR §1.56(b). Applicants do not waive any rights to take any action which would be appropriate to antedate or otherwise remove as a competent reference any document which is determined to be a *prima facie* art reference against the claims of the present application.

**TIMING OF THE DISCLOSURE**

The listed documents are being submitted in compliance with 37 CFR §1.97(b), within three (3) months of the filing date of the application.

**RELEVANCE OF EACH DOCUMENT**

An English translation of the foreign-language document(s) is not readily available. However, an English language abstract of each of the foreign language document(s) was included with the references in the parent application.

Applicants respectfully request that any listed document be considered by the Examiner and be made of record in the present application and that an initialed copy of Form PTO-1449 be returned in accordance with MPEP §609.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 CFR §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 50-2350. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 50-2350.

Respectfully submitted,

Date April 14, 2004

By Bernard P. Friedrichsen

FOLEY & LARDNER LLP  
Customer Number:

**23524**

PATENT TRADEMARK OFFICE

Telephone: (608) 258-4281

Facsimile: (608) 258-4258

Bernard P. Friedrichsen  
Attorney for Applicant  
Registration No. 44,689

| Form PTO-1449<br>(MODIFIED)  |     | U.S. DEPARTMENT OF COMMERCE<br>PATENT AND TRADEMARK OFFICE  |               | ATTY. DOCKET NO.<br>072121-0389     |       | SERIAL NO.                |                                  |
|--|-----|---|---------------|-------------------------------------|-------|---------------------------|----------------------------------|
| <b>INFORMATION DISCLOSURE CITATION</b><br><br>Date filed: April 14, 2004<br><i>(Use several sheets if necessary)</i>   |     |   |               | APPLICANT<br>Paul A. Renhowe et al. |       |                           |                                  |
|  |     |   |               | FILING DATE<br>Submitted Herewith   |       | GROUP ART UNIT<br>Unknown |                                  |
| <b>U.S. PATENT DOCUMENTS</b>   |     |   |               |                                     |       |                           |                                  |
| EXAMINER<br>INITIAL  | REF | DOCUMENT<br>NUMBER  | DATE          | NAME                                | CLASS | SUB-<br>CLASS             | FILING DATE<br>IF<br>APPROPRIATE |
|  |     | 4,882,342   | Nov. 21, 1989 | Von der Saal et al.                 |       |                           |                                  |
|  |     | 5,073,492   | Dec. 17, 1991 | Chen et al.                         |       |                           |                                  |
|  |     | 5,414,088   | May 9, 1995   | Von der Saal et al.                 |       |                           |                                  |
|  |     | 5,585,380   | Dec. 17, 1996 | Bianco et al.                       |       |                           |                                  |
|  |     | 5,646,153   | Jul. 8, 1997  | Spada et al.                        |       |                           |                                  |
|  |     | 5,710,158   | Jan. 20, 1998 | Myers et al.                        |       |                           |                                  |
|  |     | 5,763,441   | Jun. 9, 1998  | App et al.                          |       |                           |                                  |
| <b>FOREIGN PATENT DOCUMENTS</b>  |     |   |               |                                     |       |                           |                                  |
|  | REF | DOCUMENT<br>NUMBER  | DATE          | COUNTRY                             | CLASS | SUB-<br>CLASS             | TRANSLATION<br>YES NO            |
|  |     | 2363459   | Jun. 26, 1975 | Germany                             |       |                           |                                  |
|  |     | DE 3634066 A1   | July 10, 1986 | Germany                             |       |                           |                                  |
|  |     | 19841985  | Mar. 9, 2000  | Germany                             |       |                           |                                  |
|  |     | 0 290 153   | Nov. 9, 1998  | Europe                              |       |                           |                                  |
| <b>OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)</b>  |     |   |               |                                     |       |                           |                                  |
|  |     | Aprelikova, O., et al., "FLT4, a novel Class III Receptor Tyrosine Kinase in chromosome 5q33-qter1," <i>Cancer Res.</i> , Vol. 52, pp. 746-748, February 1, 1992, published by The American Association for Cancer Research, Stanford University Libraries' High Wire Press, California, United States of America.                          |               |                                     |       |                           |                                  |
|  |     | Carmeliet, P. et al., "Angiogenesis in Cancer and Other Diseases," <i>Nature</i> , 407, pp. 249-257 (2000).   |               |                                     |       |                           |                                  |
|  |     | Connolly, D., et al., "Human Vascular Permeability Factor," <i>J. Biol. Chem.</i> , Vol. 264, pp. 20017-20024, 1989, published by The American Society For Biochemistry and Molecular Biology, Inc., Stanford University Libraries' High Wire Press, California, United States of America.  |               |                                     |       |                           |                                  |
|  |     | Connolly, D., et al., "Tumor Vascular Permeability Factor Stimulates Endothelial Cell Growth and Angiogenesis," <i>J. Clin. Invest.</i> , Vol. 84, pp. 1470-1478, November, 1989, published by The American Society for Clinical Investigation, Inc., Stanford University Libraries' High Wire Press, California, United States of America. |               |                                     |       |                           |                                  |
|  |     | DeVries, C., et al., "The fms-Like Tyrosine Kinase, a Receptor for Vascular Endothelial Growth Factor," <i>Science</i> , Vol. 255, pp. 989-991, February 21, 1992, published by The American Society for the Advancement of Science, Stanford University Libraries' High Wire Press, California, United States of America.                  |               |                                     |       |                           |                                  |
| <b>EXAMINER</b>  |     |   |               | <b>DATE CONSIDERED</b>              |       |                           |                                  |
| * <b>EXAMINER:</b> Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include any copy of this form with next communication to applicant. |     |   |               |                                     |       |                           |                                  |



| Form PTO-1449<br>(MODIFIED)  |     | U.S. DEPARTMENT OF COMMERCE<br>PATENT AND TRADEMARK OFFICE |               | ATTY. DOCKET NO.<br>072121-0389     |       | SERIAL NO.                |             |    |
|--|-----|--|---------------|-------------------------------------|-------|---------------------------|-------------|----|
| <b>INFORMATION DISCLOSURE CITATION</b><br><br><i>(Use several sheets if necessary)</i> |     |  |               | APPLICANT<br>Paul A. Renhowe et al. |       |                           |             |    |
|  |     |  |               | FILING DATE<br>Submitted Herewith   |       | GROUP ART UNIT<br>Unknown |             |    |
| <b>FOREIGN PATENT DOCUMENTS</b>  |     |  |               |                                     |       |                           |             |    |
|  | REF | DOCUMENT<br>NUMBER   | DATE          | COUNTRY                             | CLASS | SUB-<br>CLASS             | TRANSLATION |    |
|  |     |  |               |                                     |       |                           | YES         | NO |
|  |     | 0 509 717  | Apr. 10, 1992 | Europe                              |       |                           |             |    |
|  |     | 0 508 800  | Oct. 14, 1992 | Europe                              |       |                           |             |    |
|  |     | 0 747 771  | Dec. 11, 1996 | Europe                              |       |                           |             |    |
|  |     | 0 797 376  | Sep. 24, 1997 | Europe                              |       |                           |             |    |
|  |     | 1 086 705  | Mar. 28, 2001 | Europe                              |       |                           |             |    |
|  |     | 6-9952   | Jan. 18, 1994 | Japan                               |       |                           |             |    |
|  |     | 7-43896  | Feb. 14, 1995 | Japan                               |       |                           |             |    |
|  |     | 8-29973  | Feb. 2, 1996  | Japan                               |       |                           |             |    |
|  |     | 63-258903  | Oct. 26, 1998 | Japan                               |       |                           |             |    |
|  |     | 92/18483   | Oct. 29, 1992 | WO                                  |       |                           |             |    |
|  |     | 92/20642   | Nov. 26, 1992 | WO                                  |       |                           |             |    |
|  |     | 95/15758   | Jun. 15, 1995 | WO                                  |       |                           |             |    |
|  |     | 95/18801   | Jul. 13, 1995 | WO                                  |       |                           |             |    |
|  |     | 97/03069   | Jan. 30, 1997 | WO                                  |       |                           |             |    |
|  |     | 97/34876   | Sep. 25, 1997 | WO                                  |       |                           |             |    |
|  |     | 97/48694   | Dec. 24, 1997 | WO                                  |       |                           |             |    |
|  |     | 98/13350   | Apr. 2, 1998  | WO                                  |       |                           |             |    |
|  |     | 99/10349   | Mar. 4, 1999  | WO                                  |       |                           |             |    |
|  |     | 99/50263   | Oct. 7, 1999  | WO                                  |       |                           |             |    |
|  |     | 99/65897   | Dec. 23, 1999 | WO                                  |       |                           |             |    |
|  |     | 00/27379   | May 18, 2000  | WO                                  |       |                           |             |    |
|  |     | 01/02369   | Jan. 11, 2001 | WO                                  |       |                           |             |    |
|  |     | 01/29025   | Apr. 26, 2001 | WO                                  |       |                           |             |    |
|  |     | 01/28993   | Apr. 26, 2001 | WO                                  |       |                           |             |    |
|  |     | 01/52904   | Jul. 26, 2001 | WO                                  |       |                           |             |    |
|  |     | 01/55114   | Aug. 2, 2001  | WO                                  |       |                           |             |    |
|  |     | 01/62251   | Aug. 30, 2001 | WO                                  |       |                           |             |    |
|  |     | 01/62252   | Aug. 30, 2001 | WO                                  |       |                           |             |    |
|  |     | 02/32861   | Apr. 25, 2002 | WO                                  |       |                           |             |    |

|   |  |   |                           |
|---|--|---|---------------------------|
| Form PTO-1449<br>(MODIFIED)   | U.S. DEPARTMENT OF COMMERCE<br>PATENT AND TRADEMARK OFFICE | ATTY. DOCKET NO.<br>072121-0389   | SERIAL NO.                |
| <b>INFORMATION DISCLOSURE CITATION</b><br><br>(Use several sheets if necessary) |  | APPLICANT<br>Paul A. Renhowe et al.   |                           |
|   |  | FILING DATE<br>Submitted Herewith   | GROUP ART UNIT<br>Unknown |
|   |  | <b>OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)</b>   |                           |
|   |  | Ferrara, N., et al., "The Biology of Vascular Endothelial Growth Factor," <i>Endocrinol. Rev.</i> , Vol. 18, No. 1, pp. 4-25, 1997, published by The Endocrine Society, Stanford University Libraries' High Wire Press, California, United States of America.   |                           |
|   |  | Folkman, J., "Fighting Cancer by Attacking Its Blood Supply," <i>Scientific American</i> , Vol. 275, pp. 150-154, September, 1996, published by Scientific American, Inc., New York, New York, United States of America.  |                           |
|   |  | Hennequin, L. F., et al., "Design and Structure - Activity Relationship of a New Class of Potent VEGF Receptor Tyrosine Kinase Inhibitors," <i>J. Med. Chem.</i> , Vol. 42, No. 26, pp. 5369-5389, 1999; published by American Chemical Society, Washington, D.C.   |                           |
|   |  | Leung, D., et al., "Vascular Endothelial Growth Factor Is a Secreted Angiogenic Mitogen," <i>Science</i> , Vol. 246, pp. 1306-1309, December 8, 1989, published by The American Society for the Advancement of Science, Stanford University Libraries' High Wire Press, California, United States of America. |                           |
|   |  | Lymboussaki, A., "Vascular endothelial growth factors and their receptors in embryos, adults, and in tumors," Academic Dissertation, University of Helsinki, Molecular/Cancer Biology Laboratory and Department of Pathology, Haartman Institute, 1999.   |                           |
|   |  | Maguire, M.P., et al., "A New Series of PDGF Receptor Tyrosine Kinase Inhibitors: 3-Substituted Quinoline Derivatives," <i>J. Med. Chem.</i> , Vol. 37, No. 14, pp. 2129-2137, 1994; published by American Chemical Society, Washington, D.C.   |                           |
|   |  | Matei, S., et al., "Condensation of ethyl 2-benzimidazoleacetate with carbonyl compounds," <i>Rev. Chim.</i> , Vol. 33, No. 6, pp. 527-530, 1989, published by the Central Institute of Chemistry, Bucharest, Romania.  |                           |
|   |  | Mustonen, T., et al., "Endothelial Receptor Tyrosine Kinases Involved in Angiogenesis," <i>J. Cell Biology</i> , Vol. 129, No. 4, pp. 895-898, May, 1995, published by The Rockefeller University Press, New York, New York, United States of America.  |                           |
|   |  | Plouet, J., et al., "Isolation and characterization of a newly identified endothelial cell mitogen produced by AtT-20 cells," <i>EMBO J.</i> , Vol. 8, No. 12, pp. 3801-3806, 1989, published by IRL Press.   |                           |
|   |  | Quinn, T., et al., "Fetal liver kinase 1 is a receptor for vascular endothelial growth factor and is selectively expressed in vascular endothelium," <i>Proc. Natl. Acad. Sci. USA</i> , Vol. 90, pp. 7533-7537, August, 1993.  |                           |
|   |  | Shibuya, M., et al., "Nucleotide sequence and expression of a novel human receptor-type tyrosine kinase gene (flt) closely related to the fms family," <i>Oncogene</i> , Vol. 5, pp. 519-524, 1990, published by Macmillan Press Ltd., Stockton Press Company, Great Britain.                                 |                           |
|   |  | Stover, D. R., "Recent advances in protein kinase inhibition: Current molecular scaffolds used for inhibitor synthesis," <i>Current Opinion in Drug Discovery &amp; Development</i> , Vol. 2, No. 4, pp. 274-285, 1999; published by PharmaPress Ltd., London, United Kingdom.                                |                           |
|   |  | Terman, B., et al., "Identification of a new endothelial cell growth factor receptor tyrosine kinase," <i>Oncogene</i> , Vol. 6, pp. 1677-1683, 1991, published by Macmillan Press Ltd., Stockton Press Company, Great Britain.   |                           |
|   |  | Ukrainets, I., "Effective Synthesis of 3-(Benzimidazol-2-yl)-4-Hydroxy-2-Oxo-1,2-Dihydroquinolines," <i>Tet. Lett.</i> , Vol. 36, No. 42, pp. 7747-7748, 1995, published by Elsevier Science Ltd., Great Britain.   |                           |
|   |  | Ukrainets, I., et al., "2-Carbethoxymethyl-4H-3,1-Benzoxazin-4-One. 3.*Condensation of o-Phenylenediamine," pp. 198-200, translated from <i>Khimiya Geterotsiklicheskikh Soedinii</i> , No. 2, pp. 239-241, February, 1992, published by Plenum Publ. Corp., London, Great Britain.                           |                           |

